## REMARKS

### I. INTRODUCTION

In response to the Office Action dated December 8, 1999, claims 1 and 4-6 have been amended. Claims 16-27 were withdrawn as directed to non-elected subject matter. Claims 1-15 remain in the application. Reconsideration of the application, as amended, is requested.

### II. CLAIM AMENDMENTS

Applicants' attorney has made amendments to the claims as indicated above. These amendments were made solely for the purpose of clarifying the language of the claims, and were not required to distinguish the claims over the prior art.

### III. RESTRICTION REQUIREMENT

Applicants appreciate the Examiner's rejoining of Groups I and II at page 2 of the Office Action. Applicants additionally acknowledge that claims 16-27 have been withdrawn from consideration as being drawn to non-elected subject matter.

### IV. REJECTIONS NOT BASED ON PRIOR ART

At pages 3-4 of the Office Action, claims 1-15 were rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. In response, Applicants have amended the claims as follows.

Claim 1 has been amended to explicitly recite that the transfected cell is cultured, in accordance with the Examiner's suggestion. Claim 1 has also been amended to change "cells" to "cell" to address the Examiner's concern regarding logical consistency. In addition, claim 1 has been amended to include the abbreviation "sIg", providing antecedent basis for this term as it appears in claim 3, addressing the Examiner's concern regarding claim 3.

Claims 4 and 5 have been amended to explicitly recite that the species referred to is a species "of an organism", to address the Examiner's question.

The Examiner alleged that the metes and bounds of claim 6 are unclear in the recitation of "congener". The term "congener" is defined in the specification at page 7, lines 16-23. This definition includes the types of changes to the sequence that are intended to fall within the scope of the claim and also defines a limit to how much the sequence can be changed. This limitation, "capable of associating with an Ig molecule" has also been explicitly introduced into amended claim 6 to provide further clarification.

The Examiner's concern regarding lack of antecedent basis for the recitation of "Ig molecule" in claims 12 and 13 in reference to claim 1 has been addressed by the amendments to claim 1 above.

Applicants therefore maintain that each of the rejections under 35 U.S.C. § 112, second paragraph, that were raised in the Office Action have been obviated by the amendments and arguments set forth above.

## V. PRIOR ART REJECTIONS

At pages 4-5 of the Office Action, claims 1-15 were rejected under 35 U.S.C. §102 as being anticipated by Weltzin (U.S. Patent No. 5,534,411). At pages 5-6 of the Office Action, claims 6, 8 and 13 were rejected under 35 U.S.C. §103(a) as being obvious in view of the combination of Weltzin, Morrison (WO 89/07142) and Krajci (Biochem. Biophys. Res. Comm. 1989, 158(3):783-789).

Applicants respectfully traverse these rejections.

The claimed invention is directed to a method of producing secretory Ig (sIg) molecules comprising transfecting a cell producing an Ig with a polynucleotide encoding secretory component (SC) to form an SC transfected Ig producing cell, and culturing the SC transfected Ig producing cell so as to produce secretory Ig molecules. This claim is supported by working examples described at pages 13-19 of the specification. These examples include details regarding: cloning of the human secretory component (SC; Example 1, p. 13); expression of cloned SC in cells secreting IgA (Example 2, p. 14); analysis of culture supernatants to confirm production of secretory Ig (Example 3, p. 14); pulse-chase experiments to analyze assembly of SC and IgA, confirming that SC was covalently linked to Ig intracellularly (Example 4, p. 14-16); and confirmation of *in vivo* stability of the secretory Ig so produced (Example 5, p. 16-19).

Weltzin discloses a monoclonal IgA antibody (HNK20) specific for respiratory syncytial virus produced by a hybridoma. Throughout the summary, detailed description, examples and claims of the Weltzin patent, the HNK20 antibodies are taught in a preferred form, "substantially pure" and "free from other immunological material" (col. 3, l. 33-35). The one exception appears in the paragraph at column 11, lines 39-59, which teaches that the disclosed HNK20 IgA antibodies "can be bound to secretory component to yield complexes with increased resistance to digestion by proteolytic enzymes." The text then goes on to list three alternative methods for achieving SC combined with polymeric IgA.

The second of these three suggestions is the statement recited in the Office Action: "the IgA-secreting hybridoma cells are transfected with an expression vector containing the cDNA for secretory component." This is a prophetic and speculative statement that is not substantiated by any data, specific teachings, examples or other evidence to provide a reasonable expectation that transfection of the hybridoma cells with a cDNA for SC would result in production of the IgA in secretory form. This wishful statement is not an enabling disclosure, and does not provide the public with the benefit of an operative invention.

As evidence of the non-enabling nature of the prophetic statement in Weltzin, Applicants direct the Examiner's attention to two references of record that reflect the state of the art of sIgA development as of 1995-1996. The Ma et al. reference (Science 268:716-719; attached herewith as Exhibit A; provided previously as Exhibit 8 of PTO Form 1449), was published in May of 1995. In the abstract and at column 2, lines 1-11, Ma et al. state that mammalian systems require two different cell types to assemble secretory antibodies. In addition, Applicants provide a copy of Lüllau et al. (J. Biol. Chem. 271(27):16300-16309; attached herewith as Exhibit B; provided previously as Exhibit 7 of PTO Form 1449), published in 1996. In the abstract and in the first paragraph at page 16300, Lüllau et al. state that secretory IgA can be made *in vitro* by combining recombinant SC and purified IgA, but cellular production requires two distinct types of cells. In the second two paragraphs of the same page, the authors go on to discuss the desirability of obtaining useful quantities of sIgA by using a method disclosed therein for purifying milligram quantities of IgA from hybridomas and binding the IgA with recombinant SC *in vitro*.

As further evidence that the state of the art of immunology at the time of the effective filing date of Weltzin was such that the cited prophetic statement in Weltzin was neither credible nor enabling, Applicants provide a Declaration Under 37 C.F.R. § 1.132 by Sherie L. Morrison, Ph.D.



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This Declaration is attached as Exhibit C, and establishes that those skilled in the art had several reasons to doubt the capability of a single cell to produce a complete secretory immunoglobulin molecule. The removal of these doubts required data demonstrating that an Ig-producing cell transfected with a vector encoding SC could successfully assemble and produce Ig in secretory form. These data were first provided by the inventors, and are disclosed in the above-identified patent application.

Thus, Applicants submit that each of claims 1-15 is allowable over the Weltzin, Morrison and Krajci references, taken alone or in combination. In view of the arguments and evidence presented herein, Applicants respectfully request withdrawal of the rejections based on sections 102 and 103.

## VI. CONCLUSION

In view of the above, it is submitted that this application is now in good order for allowance and such allowance is respectfully solicited. Should the Examiner believe minor matters still remain that can be resolved in a telephone interview, the Examiner is urged to call Applicants' undersigned attorney.

Respectfully submitted,

Sherie L. Morrison et al.

By their attorneys,

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